



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,825	01/11/2002	Yasunori Takada	56769 (71526)	2372
21874	7590	07/23/2008		
EDWARDS ANGELL PALMER & DODGE LLP				
P.O. BOX 55874				
BOSTON, MA 02205				
EXAMINER				
FISHER, ABIGAIL L				
ART UNIT		PAPER NUMBER		
1616				
MAIL DATE		DELIVERY MODE		
07/23/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/030,825

**Applicant(s)**

TAKADA ET AL.

**Examiner**

ABIGAIL FISHER

**Art Unit**

1616

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 4, 5, 7-10 and 13-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4-5, 7-10 and 13-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI-108)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

#### **DETAILED ACTION**

The examiner for your application in the USPTO has changed. Examiner Abigail Fisher can be reached at 571-270-3502.

Receipt of Request for Continued Examination and Amendments/Remarks filed on April 28 2008 is acknowledged. Claims 2-3, 6 and 11-12 were/stand cancelled. Claims 13-17 were added. Claims 1, 4-5, 7-10 and 13-17 are pending.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claim 9 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claims 9 and 17 as currently written is vague and indefinite. It unclear if two can be the number of polymers added. The claim state the base layer is composed of one or "more than two" of. It is unclear if this is a typo and the claim should really read one or more, or if the applicant intends the claim to be directed to one or "more than two."

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (US Patent No. 5340872, cited in the Office action mailed on 12/28/07).**

### **Applicant Claims**

Applicant claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Patel et al. teach a topical gel composition containing medicaments (abstract). 0.005% to about 10% medicament is specified (column 4 lines 48-49). Diclofenac is disclosed (column 4 line 67). It is taught that pharmaceutically acceptable salts can be incorporated. It is taught that utilization of the salt form of the medicament increase the water solubility or polar characteristics of the free drug which may be desirable (column 9, lines 31-43). It is taught that the compositions can include salts and buffers such as ammonium chloride (column 8 lines 13-15). It is taught that these components, buffers and salts, are included in amount from about 0.01-5% (column 9, lines 27-28). Sustained efficacy is disclosed (column 3 line 13).

### **Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)**

Patel et al. do not exemplify a formulation comprising sodium diclofenac and ammonium chloride. However, Patel et al. do list these two components as being suitable.

### **Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)**

It would have been obvious to one of ordinary skill in the art to formulate sodium diclofenac and ammonium chloride in the gel suspension of Patel et al. One of ordinary skill in the art would have been motivated to utilize sodium diclofenac because Patel et al. teach that pharmaceutically acceptable salts of the medicaments can be utilized especially when a more water soluble or polar compound is required. Patel et al. teach that one particular medicament that can be included is diclofenac. Therefore, if one desired this compound to be more water soluble then it would have been obvious to utilize the sodium salt of diclofenac. Further more, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated. It would have been obvious to one of ordinary skill in the art to include ammonium chloride because it taught as a specific salt that can be incorporated. While only sodium chloride is exemplified, One of ordinary skill in the art would have been motivated to replace sodium chloride with ammonium chloride as both are taught by Patel et al. as functional equivalents. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in utilizing ammonium chloride.

Regarding the claimed molar amounts, Patel et al. teach that the medicament can be present from 0.005% to about 10%, which corresponds to 0.016-31.43 mmol of sodium diclofenac. Patel teach salts from 0.05 to 5%, which corresponds to 0.93-93.47 mmol of ammonium chloride. These molar (or mmolar) amounts overlap with those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges

disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05**

**[R-5]**

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicants argue that Patel (1) is directed to ophthalmic formulations not percutaneously absorbable preparations. Applicants argue that (2) diclofenac is disclosed but sodium diclofenac is not taught. Applicants argue that (3) ammonium chloride is not disclosed. Applicants argue that (4) the use of salts in Patel for osmolality is not relevant to the absorbability of sodium diclofenac and subsequently not relevant to the patentability of the present claims. Applicants argue that (5) it is unlikely that ammonium chloride would be used in a sustained-release ophthalmic formulation due to the irritant properties of ammonium chloride. Applicants argue that (6) any *prima facie* case of obviousness is rebutted by evidence of the unexpected properties of the claimed preparations. The specification show the skin permeability rate of a composition with and without ammonium chloride. The composition with the ammonium chloride displayed unexpectedly superior properties and cannot be obvious.

Applicant's arguments filed April 28 2008 have been fully considered but they are not persuasive.

Regarding applicants' first argument, a recitation of the intended use of the claimed invention, percutaneously, in the instant application, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. **Note:** MPEP 2111.02 [R-3] In the instant case the obvious composition of Patel comprising ammonium chloride and sodium diclofenac is the same product as instantly claimed. Therefore, it would necessarily be able to be absorbed through the skin.

Regarding applicants second argument, Patel et al. teach that the pharmaceutically acceptable salts of the medicament can be utilized. One of ordinary skill in the art would have been motivated to utilize the salt in order to increase the water solubility or polarity of the compound as taught by Patel et al. Therefore, the sodium salt of diclofenac is taught by Patel et al.

Regarding applicants third argument, the examiner disagrees that ammonium chloride is not taught. Ammonium chloride is taught as a salt that can be incorporated in lines 15-16 of column 8. Sodium chloride is taught as a suitable salt to incorporate to change the osmolality of the formulation. It is taught, as the applicant has pointed out, that other salts include ammonium cations and chloride ions. There are three cations taught, sodium, potassium, and ammonium and nine different anions taught column 8, lines 30-36). Since it is taught earlier that ammonium chloride is a specific salt that can be include, one of ordinary skill in the art could envision utilizing ammonium chloride from the taught cations and anions disclosed.



Regarding applicants fourth argument, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Patel et al. teach compositions that can comprise sodium diclofenac and ammonium chloride.

Regarding applicants fifth argument, firstly the examiner disagrees; ammonium chloride is taught by Patel et al. therefore it would be suitable for ophthalmic formulations. Secondly, "the arguments of counsel cannot take the place of evidence in the record." *In re Schulze*, 346 F.2d 600, 145 USPQ 716, 718 (CCPA 1965), *In re Huang*, 40 USPQ 2d 1685 (Fed. Cir. 1996), *In re De Blauwe et al.*, 222 USPQ 191, (Fed. Cir. 1984). Applicant has not proved any factual evidence that the compositions cannot be utilized as ophthalmic formulations if they comprise ammonium chloride.

Regarding applicants sixth argument, the examples in the specification are not a true side by side comparison of the closest prior art. While applicant contends that a composition comprising ammonium chloride compared to that without ammonium chloride provides superior art, the prior art recognizes the addition of ammonium chloride so it would have been obvious to have added ammonium chloride, thereby resulting in the instant invention.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

**Claims 1, 4, 5, 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ledger et al. (US Patent No. 5120545, cited in the Office action mailed on 12/28/07) in view and Inagi et al. (US Patent No. 5773028, cited in the Office action mailed on 12/28/07).**

#### **Applicant Claims**

Applicant claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

#### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Ledger et al teaches a matrix for transdermal administration of a drug and an antigen processing-inhibiting agent is disclosed (abstract). 0.2%-20% weak base antigen processing-inhibiting agent of the drug is disclosed (column 9 lines 64-68). Ammonium chloride is specified (column 5 line 34). The amounts exemplified are 0, 2, 4 or 8 wt%. It is taught that the incorporation of drugs or agents are intended to have their broadest interpretation as to any therapeutically active substance which is to be delivered (column 4, lines 35-37). Therapeutic areas include analgesics and anti-inflammatories, among others (column 4, lines 42-61). One specific analgesic agents taught is ketoprofen (column 4 lines 45 and 63). An adhesive layer containing the agent and drug is specified (column 7 lines 8-9). Ointments are disclosed (column 6 line 37).

#### **Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)**

Ledger et al. do not specify that sodium diclofenac can be incorporated. However, this deficiency is cured by Inagi et al.

Inagi et al. teach that ketoprofen and sodium diclofenac are both analgesic agents (column 8, lines 1-4).

***Finding of Prima Facie Obviousness Rational and Motivation  
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art to combine the teachings of Ledger et al. and Inagi et al. and utilize sodium diclofenac. One of ordinary skill in the art would have been motivated to replace ketoprofen with sodium diclofenac as both are taught by Inagi et al. as functional equivalents. Furthermore, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

Regarding the claimed amounts of ammonium chloride, 0 to 8 wt % of ammonium chloride correlates to 0 to 0.15 mols. 0.2-20% of sodium diclofenac correlates to 0.06 mmol to 0.06 mols. Therefore, the amounts and correspond ratio overlaps with the instant claims. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Response to Arguments***

Applicants argue that (1) Ledger does not disclose diclofenac. Applicants argue that (2) Ledger mentions ammonium chloride as a weak base to raise the pH, which is not relevant to the presently claimed percutaneously absorbable preparation. Applicants argue that (3) there is no motivation to modify the teachings of Ledger as suggested by the office because there is no teaching or suggestion that a "sensitizing drug" as that term is used by Ledger. Applicants argue that (4) any *prima facie* case of obviousness is rebutted by evidence of the unexpected properties of the claimed preparations. The specification show the skin permeability rate of a composition with and without ammonium chloride. The composition with the ammonium chloride displayed unexpectedly superior properties and cannot be obvious.

Applicant's arguments filed April 28 2008 have been fully considered but they are not persuasive.

Regarding applicants first argument, the examiner recognizes that sodium diclofenac is not specifically disclosed. That is why Inagi et al. is utilized. Inagi et al. teach that sodium diclofenac and ketoprofen, a specifically disclosed drug, are functional equivalents.

Regarding applicants second argument, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Ledger et al. teach compositions that comprise ammonium chloride and a drug. The larger

disclosure of suitable drugs that can be incorporated demonstrate that the type of drug is not critical to the invention and therefore, it would have been obvious to incorporate sodium diclofenac as it is taught as a functional equivalent of specific drugs mentioned. Therefore, the instant invention would have been obvious to one of ordinary skill in the art based on the teachings of Leger et al. and Inagi et al.

Regarding applicants third argument, the examiner has indicated that there is motivation to combine. Depending on the desired symptom/condition to treat, the selection of a specific drug is *prima facie* obvious. Furthermore, Ledger et al. disclose numerous different classes of drugs that can be incorporated. This indicates that there is no criticality to the drug incorporated. Therefore, since sodium diclofenac is taught as a functional equivalent of specific drug disclosed by Ledger et al. it would have been obvious to one of ordinary skill in the art to incorporate it into the invention of Ledger et al.

Regarding applicants fourth argument, the examples in the specification are not a true side by side comparison of the closes prior art. While applicant contends that a composition comprising ammonium chloride compared to that without ammonium chloride provides superior art. The prior art teaches compositions comprising ammonium chloride. It would have been obvious to one of ordinary skill in the art to add sodium diclofenac because it is taught as a functional equivalent in the art as specified drugs and because Ledger et al. indicates that almost any drug can be incorporated. The large amounts of drugs listed indicate that the type of drug is not critical to the invention. Therefore, it would have been obvious to incorporate sodium diclofenac in the

invention of Ledger et al. and thereby resulting in the instant invention with a reasonable expectation of success.

**Claims 1, 4-5, 7-10 and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawaji et al. (US Patent No. 6262121) in view of Arellano et al. (European Journal of Pharmaceutical Sciences) and in further view of Porter et al. (US Patent No. 5968533).**

#### **Applicant Claims**

Applicant claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Applicant claims a method for improve the percutaneous absorbability of sodium diclofenac comprising proving ammonium chloride in the preparation at a range from 0.5 to 10 fold mole/mole based on the sodium diclofenac.

#### **Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Kawaji et al. teach oil patches containing diclofenac sodium and fatty acids which are combined in an adhesive (abstract). The diclofenac sodium is admixed in a solution of styrene-isoprene-styrene block copolymer (column2, lines 52-53). The amount of diclofenac sodium included is from 0.5 to 6% (column 2, lines 61-63).

#### **Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)**

Kawaji et al. do not specify utilizing ammonium chloride in the patch. However, this deficiency is cured by Arellano et al. and Porter et al.

Arellano et al. teach the inclusion of propylene glycol and isopropyl myristate on the penetration of diclofenac sodium (title). The amount of propylene glycol incorporated is from 20 to 60 % and isopropyl myristate from 3 to 5% (table 1). It is taught that these agents are penetration enhancers in the topical formulations of drugs (page 129, left column, last paragraph). It is taught that the inclusion of propylene glycol and/or isopropyl myristate provided good enhancement effects of sodium diclofenac (page 134, left column, last paragraph).

Porter et al. is directed to adhesive materials utilizing a patch to deliver active agents (abstract). It is taught that utilization of certain ingredients in the patches can increase the release rates and/or absorption rates of the active ingredients (i.e. they are penetration enhancers). Disclosed additives which increase the release rate include ethylene glycol, polyethylene glycols and ammonium chloride (column 5, lines 20-27).

***Finding of Prima Facie Obviousness Rational and Motivation  
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kawaji et al., Arellano et al., and Porter et al., and utilize ammonium chloride in the invention of Kawaji et al. One of ordinary skill in the art would have been motivated to utilize ammonium chloride because it is taught by Arellano et al. that the inclusion of penetration enhancers helps with the enhancement of sodium diclofenac

into the skin. One of ordinary skill in the art would have been motivated to replace propylene glycol with ammonium chloride as both are taught as functional equivalents.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kawaji et al., Arellano et al., and Porter et al., and utilize ammonium chloride in the invention of Kawaji et al. to improve the absorbability of sodium diclofenac. One of ordinary skill in the art would have been motivated to utilize the composition in this type of method as ammonium chloride is taught as a penetration enhancer by Porter et al. and penetration enhancers are known in the art to enhance the absorption of sodium diclofenac as taught by Arellano et al. The purpose of a penetration enhancer is to help the active agent absorb into the skin. Therefore, one of ordinary skill in the art would have a reasonable expectation that inclusion of penetration enhancers would enhance the absorbability of sodium diclofenac.

Regarding the claimed amount of ammonium chloride, Kawaji et al. teach that the amount of sodium diclofenac that can be incorporated is from 0.5 to 6%, which corresponds to 1.57 mmol to 18.85 mmol. Arellano et al. teach that the amount of penetration enhancer to be incorporated ranges from 3 to 60%, which correlates to 56.08 mmol to 1113.17 mmol. These amounts overlap with those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]** Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the



prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1, 4-5 and 7-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-21 of copending Application No. 10479072. Although the conflicting**

**claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.**

The instant application claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Copending '072 claims a percutaneously absorbable patch having an adhesive substrate layer which contains sodium diclofenac, an ammonium chloride, oleic acid and polyethylene glycol.

Copending '072 does not claim a particular amount of ammonium chloride. However, it would have been obvious to one of ordinary skill in the art to determine optimal amounts of ammonium chloride to add in the patch of copending '072. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Claims 1, 4-5, 7-10 and 13-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-21 of copending Application No. 10549184 in view of Arellano et al. and**

**in further view of Porter et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.**

The instant application claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Copending '184 claims a patch containing a non-steroidal anti-inflammatory. A specific anti-inflammatory claimed is diclofenac and its pharmacological acceptable salt.

Copending '184 does not claim the addition of ammonium chloride. However, this deficiency is cured by Arellano et al. and Porter et al.

Arellano et al. teach the include of propylene glycol and isopropyl myristate on the penetration of diclofenac sodium (title). The amount of propylene glycol incorporated is from 20 to 60 % and isopropyl myristate from 3 to 5% (table 1). It is taught that these agents are penetration enhancer in the topical formulations of drugs (page 129, left column, last paragraph). It is taught that the inclusion of propylene glycol and/or isopropyl myristate provided good enhancement effects of sodium diclofenac (page 134, left column, last paragraph).

Porter et al. is directed to adhesive materials utilizing a patch to deliver active agents (abstract). It is taught that utilization of certain ingredients in the patches can increase the release rates and/or absorption rates of the active ingredients (i.e. they are penetration enhancers). Disclosed additives which increase the release rate include ethylene glycol, polyethylene glycols and ammonium chloride (column 5, lines 20-27).

It would have been obvious to one of ordinary skill in the art to combine the teachings of copending '184, Arellano et al., and Porter et al. and utilize ammonium chloride to enhance the penetration of diclofenac sodium. One of ordinary skill in the art would have been motivated to utilize ammonium chloride in the composition of copending '184 and subsequently the composition in instant type of method as ammonium chloride is taught as a penetration enhancer by Porter et al. and penetration enhancers are known in the art to enhance the absorption of sodium diclofenac as taught by Arellano et al. The purpose of a penetration enhancer is to help the active agent absorb into the skin. Therefore, one of ordinary skill in the art would have a reasonable expectation that inclusion of penetration enhancers would enhance the absorbability of sodium diclofenac.

Regarding the claimed amount of ammonium chloride, copending '184 claims that the amount of sodium diclofenac that can be incorporated is from 1-25 %, which corresponds to 3.19 mmol to 78.6 mmol. Arellano et al. teach that the amount of penetration enhancer to be incorporated ranges from 3 to 60%, which correlates to 56.08 mmol to 1113.17 mmol. These amounts overlap with those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]** Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

This is a provisional obviousness-type double patenting rejection.

**Claims 1, 4-5, 7-10 and 13-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 10/548739 in view of Arellano et al. and in further view of Porter et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.**

The instant application claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Copending '739 claims a patch comprising an anti-inflammatory. Polymers are claimed as being included. A specific anti-inflammatory claimed is diclofenac and its pharmaceutically acceptable salt.

Copending '739 does not claim the addition of ammonium chloride. However, this deficiency is cured by Arellano et al. and Porter et al.

The teachings of Arellano et al. and Porter et al. are set forth above.

It would have been obvious to one of ordinary skill in the art to combine the teachings of copending '739, Arellano et al., and Porter et al. and utilize ammonium chloride to enhance the penetration of diclofenac sodium. One of ordinary skill in the art

would have been motivated to utilize ammonium chloride in the composition of copending '739 and subsequently the composition in the instant method as ammonium is taught as a penetration enhancer by Porter et al. and penetration enhancers are known in the art to enhance the absorption of sodium diclofenac as taught by Arellano et al. The purpose of a penetration enhancer is to help the active agent absorb into the skin. Therefore, one of ordinary skill in the art would have a reasonable expectation that inclusion of penetration enhancers would enhance the absorbability of sodium diclofenac.

Regarding the claimed amount of ammonium chloride, Arellano et al. teach that the amount of penetration enhancer to be incorporated ranges from 3 to 60%, which correlates to 56.08 mmol to 1113.17 mmol. Copending '739 does not claim a specific amount of active, however, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

This is a provisional obviousness-type double patenting rejection.

**Claims 1, 4-5, 7-10 and 13-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 11596605 in view of Arellano et al. and**

**in further view Porter et al.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.

The instant application claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Copending '605 claims a percutaneous preparation comprising a non-steroidal anti-inflammatory analgesic. A specific analgesic claimed is diclofenac and its pharmaceutically acceptable salt.

Copending '605 does not claim the addition of ammonium chloride. However, this deficiency is cured by Arellano et al. and Porter et al.

The teachings of Arellano et al. and Porter et al. are set forth above.

It would have been obvious to one of ordinary skill in the art to combine the teachings of copending '605, Arellano et al., and Porter et al. and utilize ammonium chloride to enhance the penetration of diclofenac sodium. One of ordinary skill in the art would have been motivated to utilize ammonium chloride in the composition of copending '605 and subsequently the composition in instant method as ammonium is taught as a penetration enhancer by Porter et al. and penetration enhancers are known in the art to enhance the absorption of sodium diclofenac as taught by Arellano et al. The purpose of a penetration enhancer is to help the active agent absorb into the skin. Therefore, one of ordinary skill in the art would have a reasonable expectation that inclusion of penetration enhancers would enhance the absorbability of sodium diclofenac.

Regarding the claimed amount of ammonium chloride, copending '605 claims that the amount of sodium diclofenac that can be incorporated is from 0.1 to 10 %, which corresponds to 0.314 mmol to 31.4 mmol. Arellano et al. teach that the amount of penetration enhancer to be incorporated ranges from 3 to 60%, which correlates to 56.08 mmol to 1113.17 mmol. These amounts overlap with those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]** Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

This is a provisional obviousness-type double patenting rejection.

**Claims 1, 4-5, 7-10 and 13-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 13 -15 of copending Application No. 10258022 in view of Arellano et al. and in further view Porter et al.** Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.



The instant application claims a preparation comprising sodium diclofenac and ammonium chloride, wherein the ammonium chloride is blended at the range of from 0.5 to 10 fold (mole/mole) based on the sodium diclofenac.

Copending '022 claims a plaster having adhesion to the skin consisting essentially of a styrene-isoprene-styrene block copolymer and 0.1 to 8% of an anti-inflammatory. A specific anti-inflammatory claimed is diclofenac.

Copending '022 does not claim the addition of ammonium chloride. However, this deficiency is cured by Arellano et al. and Porter et al.

The teachings of Arellano et al. and Porter et al. are set forth above.

It would have been obvious to one of ordinary skill in the art to combine the teachings of copending '022, Arellano et al., and Porter et al. and utilize ammonium chloride to enhance the penetration of diclofenac sodium. One of ordinary skill in the art would have been motivated to utilize ammonium chloride in the composition of copending '022 and subsequently the composition in the instant method as ammonium is taught as a penetration enhancer by Porter et al. and penetration enhancers are known in the art to enhance the absorption of sodium diclofenac as taught by Arellano et al. The purpose of a penetration enhancer is to help the active agent absorb into the skin. Therefore, one of ordinary skill in the art would have a reasonable expectation that inclusion of penetration enhancers would enhance the absorbability of sodium diclofenac.

Regarding the claimed amount of ammonium chloride, copending '605 claims that the amount of sodium diclofenac that can be incorporated is from 0.1 to 8 %, which

corresponds to 0.314 mmol to 25.14 mmol. Arellano et al. teach that the amount of penetration enhancer to be incorporated ranges from 3 to 60%, which correlates to 56.08 mmol to 1113.17 mmol. These amounts overlap with those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]** Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

This is a provisional obviousness-type double patenting rejection.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher  
Examiner  
Art Unit 1616

AF

/Mina Haghighatian/  
Primary Examiner, Art Unit 1616